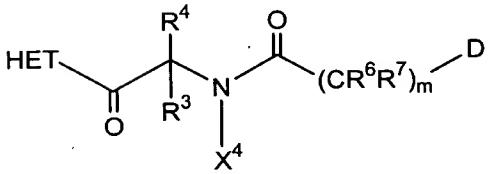
Amendments to the Claims

Claim 1 (amended) A compound of the formula



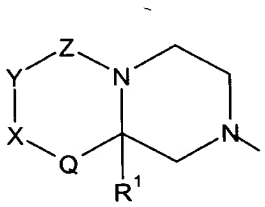
I

or a stereoisomeric mixture thereof, diastereomerically enriched, diastereomerically pure, enantiomerically enriched or enantiomerically pure isomer thereof, or a prodrug of such compound, mixture or isomer thereof, or a pharmaceutically acceptable salt of the compound, mixture, isomer or prodrug,

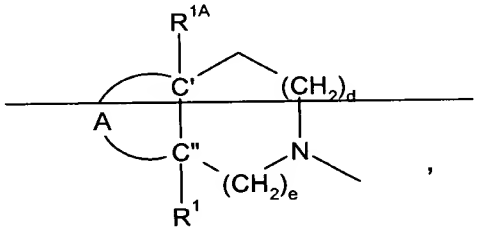
wherein:

m is 0, 1 or 2;

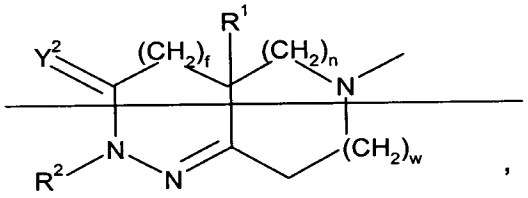
HET is a heterocyclic moiety selected from the group consisting of



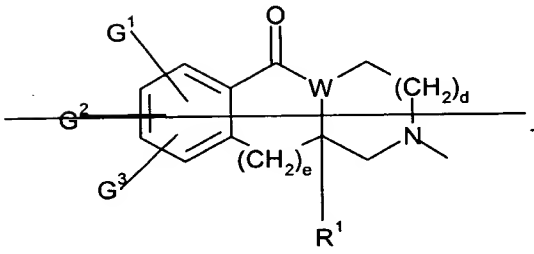
,



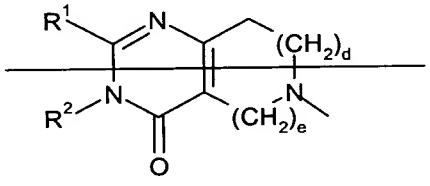
,



,



and



;

~~d is 0, 1 or 2;~~

~~e is 1 or 2;~~

~~f is 0 or 1;~~

~~n and w are 0, 1 or 2, provided that n and w cannot both be 0 at the same time;~~

~~Y^2 is oxygen or sulfur;~~

~~A is a radical, where the left hand side of the radical as shown below is connected to C" and the right hand side of the radical as shown below is connected to C', selected from the group consisting of $-NR^2-C(O)-NR^2-$, $-NR^2-S(O)_2-NR^2-$, $-O-C(O)-NR^2-$, $-NR^2-C(O)-O-$, $-C(O)-NR^2-C(O)-$, $-C(O)-NR^2-C(R^9R^{10})-$, $-C(R^9R^{10})-NR^2-C(O)-$, $-C(R^9R^{10})-C(R^9R^{10})-C(R^9R^{10})-$, $-S(O)_2-C(R^9R^{10})-C(R^9R^{10})-$, $-C(R^9R^{10})-O-C(O)-$, $-C(R^9R^{10})-O-C(R^9R^{10})-$, $-NR^2-C(O)-C(R^9R^{10})-$, $-O-C(O)-C(R^9R^{10})-$, $-C(R^9R^{10})-C(O)-NR^2-$, $-C(O)-NR^2-C(O)-$, $-C(R^9R^{10})-C(O)-O-$, $-C(O)-NR^2-C(R^9R^{10})-C(R^9R^{10})-$, $-C(O)-O-C(R^9R^{10})-$, $-C(R^9R^{10})-C(R^9R^{10})-C(R^9R^{10})-C(R^9R^{10})-$, $-S(O)_2-NR^2-C(R^9R^{10})-C(R^9R^{10})-$, $-C(R^9R^{10})-C(R^9R^{10})-NR^2-C(O)-$, $-C(R^9R^{10})-C(R^9R^{10})-O-C(O)-$, $-NR^2-C(O)-C(R^9R^{10})-C(R^9R^{10})-$, $-NR^2-S(O)_2-C(R^9R^{10})-C(R^9R^{10})-$, $-O-C(O)-C(R^9R^{10})-C(R^9R^{10})-$, $-C(R^9R^{10})-C(R^9R^{10})-C(O)-NR^2-$, $-C(R^9R^{10})-C(R^9R^{10})-C(O)-$, $-C(R^9R^{10})-NR^2-C(O)-O-$, $-C(R^9R^{10})-O-C(O)-NR^2-$, $-C(R^9R^{10})-NR^2-C(O)-NR^2-$, $-NR^2-C(O)-O-C(R^9R^{10})-$, $-NR^2-C(O)-NR^2-C(R^9R^{10})-$, $-NR^2-S(O)_2-NR^2-C(R^9R^{10})-$, $-O-C(O)-NR^2-C(R^9R^{10})-$, $-C(O)-N=C(R^{11})-NR^2-$, $-C(O)-NR^2-C(R^{11})=N-$, $-C(R^9R^{10})-NR^{12}-C(R^9R^{10})-$, $-NR^{12}-C(R^9R^{10})-$, $-NR^{12}-C(R^9R^{10})-C(R^9R^{10})-$, $-C(O)-O-C(R^9R^{10})-C(R^9R^{10})-$, $-NR^2-C(R^{11})=N-C(O)-$, $-C(R^9R^{10})-C(R^9R^{10})-N(R^{12})-$, $-C(R^9R^{10})-NR^{12}-$, $-N=C(R^{11})-NR^2-C(O)-$, $-C(R^9R^{10})-C(R^9R^{10})-NR^2-S(O)_2-$, $-C(R^9R^{10})-C(R^9R^{10})-S(O)_2-NR^2-$, $-C(R^9R^{10})-C(R^9R^{10})-C(O)-O-$, $-C(R^9R^{10})-S(O)_2-C(R^9R^{10})-$, $-C(R^9R^{10})-C(R^9R^{10})-S(O)_2-$, $-O-C(R^9R^{10})-C(R^9R^{10})-$, $-C(R^9R^{10})-C(R^9R^{10})-O-$, $-C(R^9R^{10})-C(O)-C(R^9R^{10})-$, $-C(O)-C(R^9R^{10})-C(R^9R^{10})-$ and $-C(R^9R^{10})-NR^2-S(O)_2-NR^2-$;~~

Q is a covalent bond or CH_2;

~~W is CH or N;~~

X is CR^9R^{10}, $C=CH_2$ or C=O;

Y is CR^9R^{10}, O or NR^2;

Z is C=O, C=S or $S(O)_2$;

~~G^1 is hydrogen, halo, hydroxy, nitro, amino, cyano, phenyl, carboxyl, $CONH_2$, (C_1-C_4)alkyl optionally independently substituted with one or more phenyl, one or more halogens or one or more hydroxy groups, (C_1-C_4)alkoxy optionally independently substituted with one or more phenyl, one or more halogens or one or more hydroxy groups, (C_1-C_4)alkylthio, phenoxy, $COO(C_1-C_4)$alkyl, N,N-di-(C_1-C_4)alkylamino, (C_2-C_6)alkenyl optionally independently substituted with one or more phenyl, one or more halogens or one or more hydroxy groups, (C_2-C_6)alkynyl optionally independently substituted with one or more phenyl, one or more halogens or one or more hydroxy groups, (C_3-C_6)cycloalkyl optionally~~

~~independently substituted with one or more $(C_1$-$C_4)$alkyl groups, one or more halogens or one or more hydroxy groups, $(C_1$-$C_4)$alkylamino carbonyl or di-$(C_1$-$C_4)$alkylamino carbonyl;~~

~~G^2 and G^3 are each independently selected from the group consisting of hydrogen, halo, hydroxy, $(C_1$-$C_4)$alkyl optionally independently substituted with one to three halogens and $(C_1$-$C_4)$alkoxy optionally independently substituted with one to three halogens;~~

R^1 is hydrogen, -CN, $-(CH_2)_qN(X^6)C(O)X^6$, $-(CH_2)_qN(X^6)C(O)(CH_2)_t$-$A^1$, $-(CH_2)_qN(X^6)S(O)_2(CH_2)_t$-$A^1$, $-(CH_2)_qN(X^6)S(O)_2X^6$, $-(CH_2)_qN(X^6)C(O)N(X^6)(CH_2)_t$-$A^1$, $-(CH_2)_qN(X^6)C(O)N(X^6)(X^6)$, $-(CH_2)_qC(O)N(X^6)(X^6)$, $-(CH_2)_qC(O)N(X^6)(CH_2)_t$-$A^1$, $-(CH_2)_qC(O)OX^6$, $-(CH_2)_qC(O)O(CH_2)_t$-A^1, $-(CH_2)_qOX^6$, $-(CH_2)_qOC(O)X^6$, $-(CH_2)_qOC(O)(CH_2)_t$-A^1, $-(CH_2)_qOC(O)N(X^6)(CH_2)_t$-$A^1$, $-(CH_2)_qOC(O)N(X^6)(X^6)$, $-(CH_2)_qC(O)X^6$, $-(CH_2)_qC(O)(CH_2)_t$-A^1, $-(CH_2)_qN(X^6)C(O)OX^6$, $-(CH_2)_qN(X^6)S(O)_2N(X^6)(X^6)$, $-(CH_2)_qS(O)_mX^6$, $-(CH_2)_qS(O)_m(CH_2)_t$-A^1, $-(C_1$-$C_{10})$alkyl, $-(CH_2)_t$-A^1, $-(CH_2)_q$-$(C_3$-$C_7)$cycloalkyl, $-(CH_2)_q$-Y^1-$(C_1$-$C_6)$alkyl, $-(CH_2)_q$-Y^1-$(CH_2)_t$-A^1 or $-(CH_2)_q$-Y^1-$(CH_2)_t$-$(C_3$-$C_7)$cycloalkyl;

where the alkyl and cycloalkyl groups in the definition of R^1 are optionally substituted with $(C_1$-$C_4)$alkyl, hydroxy, $(C_1$-$C_4)$alkoxy, carboxyl, $-CONH_2$, $-S(O)_m(C_1$-$C_6)$alkyl, $-CO_2(C_1$-$C_4)$alkyl ester, 1H-tetrazol-5-yl or 1, 2 or 3 fluoro groups;

Y^1 is O, $S(O)_m$, $-C(O)NX^6$-, -CH=CH-, -C≡C-, $-N(X^6)C(O)$-, $-C(O)NX^6$-, -C(O)O-, $-OC(O)N(X^6)$- or -OC(O)-;

q is 0, 1, 2, 3 or 4;

t is 0, 1, 2 or 3;

said $(CH_2)_q$ group and $(CH_2)_t$ group in the definition of R^1 are optionally independently substituted with hydroxy, $(C_1$-$C_4)$alkoxy, carboxyl, $-CONH_2$, $-S(O)_m(C_1$-$C_6)$alkyl, $-CO_2(C_1$-$C_4)$alkyl ester, 1H-tetrazol-5-yl, 1, 2 or 3 fluoro groups or 1 or 2 $(C_1$-$C_4)$alkyl groups;

~~R^{1A} is selected from the group consisting of hydrogen, F, Cl, Br, I, $(C_1$-$C_6)$alkyl, phenyl$(C_1$-$C_3)$alkyl, pyridyl$(C_1$-$C_3)$alkyl, thiazolyl$(C_1$-$C_3)$alkyl and thienyl$(C_1$-$C_3)$alkyl, provided that R^{1A} is not F, Cl, Br or I when a heteroatom is vicinal to C";~~

~~R^2, for each occurrence, is independently hydrogen, $(C_1$-$C_8)$alkyl, $(C_0$-$C_3)$alkyl-$(C_3$-$C_8)$cycloalkyl, $(C_1$-$C_4)$alkyl-A^1 or A^1;~~

~~where the alkyl groups and the cycloalkyl groups in the definition of R^2 are optionally substituted with hydroxy, $C(O)OX^6$, $C(O)N(X^6)(X^6)$, $N(X^6)(X^6)$,~~

~~$-S(O)_m(C_1-C_6)$alkyl, $-C(O)A^1$, $-C(O)(X^6)$, $-CF_3$, -CN or 1, 2 or 3 independently selected halogens;~~

R^3 and R^4 are each independently selected from the group consisting of hydrogen, (C_1-C_8)alkyl, $-CH(R^8)$-aryl, $-CH(R^8)$-heteroaryl, $-(C_0-C_3)$alkyl(C_3-C_8)cycloalkyl, wherein the aryl or heteroaryl groups are optionally substituted by one or two R^b groups;

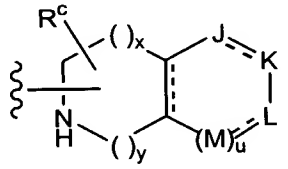
R^b, for each occurrence independently, is R^c, halo, $-OR^c$, $-NHSO_2R^c$, $-N(R^c)_2$, -CN, $-NO_2$, $-SO_2N(R^c)_2$, $-SO_2R^c$, $-CF_3$, $-OCF_3$; $-OCF_2H$ or two R^b groups attached to adjacent carbon atoms taken together to form methylenedioxy;

R^c, for each occurrence independently, is hydrogen, $-(C_1-C_8)$alkyl, $-(C_0-C_3)$alkylaryl, $-(C_0-C_3)$alkylheteroaryl, (C_3-C_6)cycloalkyl; or 2 R^b taken together with the nitrogen atom to which they are attached to form a 5- or 6- membered ring optionally containing an additional heteroatom selected from O, S or NR^3;

R^6 and R^7 are each independently selected from hydrogen, (C_1-C_6)alkyl, $-(C_0-C_3)$alkylaryl, $-(C_0-C_3)$alkylheteroaryl, $-(C_0-C_3)$alkyl(C_3-C_8)cycloalkyl;

or R^6 and R^7 together with the nitrogen atom to which they are attached form a 5- or 6-membered ring optionally containing an additional heteroatom selected from O, S, NR^3;

D is $-(C_0-C_6)$alkyl-amino-$C(=NR^7)-NR^{15}R^{16}$, $-(C_0-C_6)$alkylaminopyridyl, $-(C_0-C_6)$alkylaminoimidazolyl, $-(C_0-C_6)$alkylaminothiazolyl, $-(C_0-C_6)$alkylaminopyrimidinyl, (C_0-C_6)alkylaminopiperazinyl-R^{15}, $-(C_0-C_6)$alkylmorpholinyl, wherein R^{15} and R^{16} are independently hydrogen, $-(C_1-C_6)$alkyl, $-(C_0-C_3)$alkylaryl, $-(C_0-C_3)$alkylheteroaryl, $-(C_0-C_3)$alkyl(C_3-C_8)cycloalkyl, wherein the alkyl and aryl groups are optionally substituted with one or two R^b groups; or D is a group of the formula



wherein the dashed lines represent optional double bonds;

u is 0 or 1;

x and y are each independently 0, 1 or 2;

J, K, L and M are each independently selected from $C(R^b)_r$, N, S or O wherein R^b and R^c are as defined above and r is 1 or 2;

X^4 is hydrogen or $(C_1\text{-}C_6)$alkyl or X^4 is taken together with R^4 and the nitrogen atom to which X^4 is attached and the carbon atom to which R^4 is attached and form a five to seven membered ring;

R^8 is hydrogen, $-(C_1\text{-}C_8)$alkyl, $-(C_0\text{-}C_3)$alkylaryl, $-(C_0\text{-}C_3)$alkylheteroaryl, $-(C_3\text{-}C_6)$cycloalkyl; or 2 R^b taken together with the nitrogen atom to which they are attached to form a 5- or 6- membered ring optionally containing an additional heteroaryl selected from O, S or NR^3;

R^9 and R^{10}, for each occurrence, are each independently selected from the group consisting of hydrogen, fluoro, hydroxy and $(C_1\text{-}C_5)$alkyl optionally independently substituted with 1-5 halogens;

R^{11} is selected from the group consisting of $(C_1\text{-}C_5)$alkyl and phenyl optionally substituted with 1-3 substituents each independently selected from the group consisting of $(C_1\text{-}C_5)$alkyl, halo and $(C_1\text{-}C_5)$alkoxy;

R^{12} is selected from the group consisting of $(C_1\text{-}C_5)$alkylsulfonyl, $(C_1\text{-}C_5)$alkanoyl and $(C_1\text{-}C_5)$alkyl where the alkyl portion is optionally independently substituted by 1-5 halogens;

A^1 for each occurrence is independently selected from the group consisting of $(C_5\text{-}C_7)$cycloalkenyl, phenyl, a partially saturated, fully saturated or fully unsaturated 4- to 8-membered ring optionally having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur and nitrogen and a bicyclic ring system consisting of a partially saturated, fully unsaturated or fully saturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen, fused to a partially saturated, fully saturated or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen;

A^1 for each occurrence is independently optionally substituted, on one or optionally both rings if A^1 is a bicyclic ring system, with up to three substituents, each substituent independently selected from the group consisting of F, Cl, Br, I, $-OCF_3$, $-OCF_2H$, $-CF_3$, $-CH_3$, $-OCH_3$, $-OX^6$,
$-C(O)N(X^6)(X^6)$, $-C(O)OX^6$, oxo, $(C_1\text{-}C_6)$alkyl, nitro, cyano, benzyl,
$-S(O)_m(C_1\text{-}C_6)$alkyl, 1H-tetrazol-5-yl, phenyl, phenoxy, phenylalkyloxy, halophenyl, methylenedioxy, $-N(X^6)(X^6)$, $-N(X^6)C(O)(X^6)$, $-S(O)_2N(X^6)(X^6)$,
$-N(X^6)S(O)_2$-phenyl, $-N(X^6)S(O)_2X^6$, $-CONX^{11}X^{12}$, $-S(O)_2NX^{11}X^{12}$,

$-NX^6S(O)_2X^{12}$, $-NX^6CONX^{11}X^{12}$, $-NX^6S(O)_2NX^{11}X^{12}$, $-NX^6C(O)X^{12}$, imidazolyl, thiazolyl and tetrazolyl, provided that if A^1 is optionally substituted with methylenedioxy then it can only be substituted with one methylenedioxy;

where X^{11}, for each occurrence, is independently hydrogen or optionally substituted $(C_1\text{-}C_6)$alkyl;

the optionally substituted $(C_1\text{-}C_6)$alkyl defined for X^{11} is optionally independently substituted with phenyl, phenoxy, $(C_1\text{-}C_6)$alkoxycarbonyl, $-S(O)_m(C_1\text{-}C_6)$alkyl, 1 to 5 halogens, 1 to 3 hydroxy groups, 1 to 3 $(C_1\text{-}C_{10})$alkanoyloxy groups or 1 to 3 $(C_1\text{-}C_6)$alkoxy groups;

X^{12}, for each occurrence, is independently hydrogen, $(C_1\text{-}C_6)$alkyl, phenyl, thiazolyl, imidazolyl, furyl or thienyl, provided that when X^{12} is not hydrogen, the X^{12} group is optionally substituted with one to three substituents independently selected from the group consisting of Cl, F, CH_3, OCH_3, OCF_3 and CF_3;

or X^{11} and X^{12} are taken together to form $-(CH_2)_g\text{-}L^1\text{-}(CH_2)_g$-;

L^1 is $C(X^2)(X^2)$, O, $S(O)_m$ or $N(X^2)$;

g for each occurrence is independently 1, 2 or 3;

X^2 for each occurrence is independently hydrogen, optionally substituted $(C_1\text{-}C_6)$alkyl or optionally substituted $(C_3\text{-}C_7)$cycloalkyl, where the optionally substituted $(C_1\text{-}C_6)$alkyl and optionally substituted $(C_3\text{-}C_7)$cycloalkyl in the definition of X^2 are optionally independently substituted with $-S(O)_m(C_1\text{-}C_6)$alkyl, $-C(O)OX^3$, 1 to 5 halogens or 1-3 OX^3 groups;

X^3 for each occurrence is independently hydrogen or $(C_1\text{-}C_6)$alkyl;

X^6 for each occurrence is independently hydrogen, optionally substituted $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$halogenated alkyl, optionally substituted $(C_3\text{-}C_7)$cycloalkyl, $(C_3\text{-}C_7)$-halogenated cycloalkyl, where optionally substituted $(C_1\text{-}C_6)$alkyl and optionally substituted $(C_3\text{-}C_7)$cycloalkyl in the definition of X^6 is optionally independently mono- or di-substituted with $(C_1\text{-}C_4)$alkyl, hydroxy, $(C_1\text{-}C_4)$alkoxy, carboxyl, $CONH_2$,
$-S(O)_m(C_1\text{-}C_6)$alkyl, carboxylate $(C_1\text{-}C_4)$alkyl ester or 1H-tetrazol-5-yl; or
when there are two X^6 groups on one atom and both X^6 are independently $(C_1\text{-}C_6)$alkyl, the two $(C_1\text{-}C_6)$alkyl groups may be optionally joined and, together with the atom to which the two X^6 groups are attached, form a 4- to 9- membered ring optionally having oxygen, sulfur or NX^7 as a ring member;

X^7 is, for each occurrence independently, hydrogen or $(C_1\text{-}C_6)$alkyl optionally substituted with hydroxy;

m for each occurrence is independently 0, 1 or 2;

with the proviso that: X^6 and X^{12} cannot be hydrogen when attached to C(O) or $S(O)_2$ in the form $C(O)X^6$, $C(O)X^{12}$, $S(O)_2X^6$ or $S(O)_2X^{12}$.

Claims 2 – 11 cancelled.

Claim 12 (amended) A compound according to claim ~~11~~ 1, wherein Q is a covalent bond; X and Z are each C=O; and Y is NR^2.

Claim 13 (original) A compound according to claim 12, wherein R^2 is $(C_1\text{-}C_6)$alkyl optionally substituted by halo, and R^1 is aryl$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkyl or heteroaryl $(C_1\text{-}C_6)$alkyl wherein aryl and heteroaryl are optionally substituted with one or two groups from the following list: halo, OR^c, $-NHSO_2R^c$, $N(R^c)_2$, CN, NO_2, $SO_2N(R^c)_2$, $-SO_2R^c$, $-CF_3$, $-OCF_3$, $-OCF_2H$.

Claim 14 (original) A compound according to claim 13, wherein J, K, L and M are each N or CR^b and the dashed lines represent double bonds, R^1 is benzyl optionally substituted by halo, - R^c, $-OR^c$, $-OCF_3$, $-OCF_2H$, and R^c is hydrogen, $-(C_1\text{-}C_8)$alkyl, $-(C_0\text{-}C_3)$akylaryl, $-(C_0\text{-}C_3)$alkylheteroaryl or $-(C_3\text{-}C_6)$cycloalkyl.

Claim 15 (original) A compound according to claim 1, wherein said compound is selected from the group consisting of:

1,2,3,4-Tetrahydro-isoquinoline-(S)3-carboxylic acid {(R)1-(4-chloro-benzyl)-2-[1,3-dioxo-(S)8a-pyridin-2-ylmethyl-2-(2,2,2-trifluoro-ethyl)-hexahydro-imidazo[1,5-a]pyrazin-7-yl]-2-oxo-ethyl}-amide;

1,2,3,4-Tetrahydro-isoquinoline-(R)3-carboxylic acid {(R)1-(4-chloro-benzyl)-2-[(R)8a-(4-fluoro-benzyl)-2-methyl-1,3-dioxo-hexahydro-imidazo[1,5-a]pyrazin-7-yl]-2-oxo-ethyl}-amide;

1,2,3,4-Tetrahydro-isoquinoline-(S)3-carboxylic acid {(R)1-(4-chloro-benzyl)-2-[1,3-dioxo-(S)8a-pyridin-3-ylmethyl-2-(2,2,2-trifluoro-ethyl)-hexahydro-imidazo[1,5-a]pyrazin-7-yl]-2-oxo-ethyl}-amide;

1,2,3,4-Tetrahydro-isoquinoline-(S)3-carboxylic acid {(R)1-(4-chloro-benzyl)-2-[8a-(4-fluoro-benzyl)-3-oxo-tetrahydro-oxazolo[3,4-a]pyrazin-7-yl]-2-oxo-ethyl}-amide;

1,2,3,4-Tetrahydro-isoquinoline-(S)3-carboxylic acid {(R)1-(4-chloro-benzyl)-2-[8a-(4-fluoro-benzyl)-2-methyl-1,3-dioxo-hexahydro-imidazo[1,5-a]pyrazin-7-yl]-2-oxo-ethyl}-amide; and

1,2,3,4-Tetrahydro-isoquinoline-(S)3-carboxylic acid {(R)1-(4-chloro-benzyl)-2-[8a-(4-fluoro-benzyl)-2-methyl-1,3-dioxo-hexahydro-imidazo[1,5-a]pyrazin-7-yl]-2-oxo-ethyl}-amide.

Claim 16 (original) A compound according to claim 13, wherein J, K, L and M are each NR^b or $C(R^b)_2$ and the dashed lines represent single bonds, R^b is hydrogen, halo, R^c, OR^c, $-CF_3$, $-OCF_3$, $-OCF_2H$, R^c is hydrogen, $-(C_1-C_8)$akyl, $-(C_0-C_3)$alkylaryl, $-(C_0-C_3)$alkylheteroaryl or $-(C_3-C_6)$cycloalkyl.

Claims 17 – 28 cancelled.